REMARKS

Status of the Claims.

Claims 1-9, 12-18, and 20-26 are pending with entry of this amendment, claims 10, 11, and 19 being previously cancelled and no claims being added herein. Claims 1 and 17 are amended herein. These amendments introduce no new matter. Support is replete throughout the specification (*e.g.,* paragraph 0023 at pages 5-6, paragraph 0029 at page on page 6, and the like).

Information Disclosure Statement.

An Information Disclosure Statement (IDS) is provided herewith. The references cited on accompanying form PTO-1449 are being called to the attention of the Examiner. It is respectfully requested that the cited information be expressly considered during the prosecution of this application and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

No inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

35 U.S.C. §103(a).

Claims 1-6, 9, 12-14, 16-18, 20-23, and 25-26 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Yu *et al.* (U.S. Patent 5,385,938), in view of Poli *et al.* (1979) *Food Chemistry*, 4(3): 251-258, Wenninger (International Cosmetic Ingredient Dictionary and Handbook, 7th Ed., 1: 163-168, and Merck Index 11th ed. (1989) Glycolic acid monograph 4394, page 439. According to the Examiner, Yu *et al.* teaches a topical composition with glycolic acid as the active ingredient and ethanol as the solvent. Poli *et al.* is cited as allegedly teaching that glycolic acid is virucidal against herpes virus. Wenninger is cited as allegedly teaching that butylene glycol is useful as a solvent in numerous cosmetic marketed products. The Merck index allegedly teaches that the pH of 0.5% glycolic acid solution is 2.50. Applicants traverse by argument and amendment.

The Examiner is respectfully reminded that **a reference must be taken for all that it fairly teaches**. Once cannot "pick and choose from any one reference only so much as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. *In re Lunsford* 148 USPQ 721 (CCPA 1966) citing *In*

re Wesslau, 147 USPQ 391, 393 (CCPA 1965). Moreover, it is well recognized that "**if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification**. MPEP §2143.01, *citing In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984).

In the instant case, Yu *et al.* taken with Poli *et al.* leads one of skill away from the presently claimed invention. Claim 1 is directed to:

> 1. **A method for preventing lesions** caused by a virus of the Herpesviridae or Poxviridae family, comprising **applying to an area of the skin** a composition consisting of a pharmaceutically acceptable carrier, a C1, a C2, or a C3 alcohol or a C2, C3, or C4 diol having a concentration of 0.2 to 13.0% by volume in water, and a sufficient amount of an acid to adjust the pH of said composition to between **2.45 and 4.6**, wherein **said composition is applied during symptoms of pain, itching, burning, or tingling**.

Claim 17 recites similar language.

None of the cited references lead one of skill to conclude or expect that a formulation as recited in the claims can be used in a method for **preventing lesions.**

Moreover, contrary to the Examiner's assertion, the cited references fail to establish that formulation as recited in the pending claims has antiviral activity. Yu *et al.* offers no teaching that glycolic acid (or any other formulation disclosed therein) has antiviral activity. To the contrary, Yu *et al.* leads one of skill to compositions for the treatment of skin conditions characterized by keratoses and/or pigment changes:

> The cosmetic conditions and dermatologic disorders in humans and animals, in which the amphoteric compositions containing the dimeric or polymeric forms of hydroxyacids may be useful, include **dry skin, dandruff, acne, keratoses, psoriasis, eczema, pruritus, age spots, lentigines, melasmas, wrinkles, warts, blemished skin, hyperpigmented skin, hyperkeratotic skin, inflammatory dermatoses, skin changes associated with aging and as skin cleansers**. [emphasis added] (col. 3, lines 28-37)

While warts are mentioned in the cited language Yu *et al.* does not teach that the compounds recited therein are antiviral. Moreover, in the context of the other conditions recited (*e.g.*, hyperkeratotic skin, dry skin, dandruff, keratoses, psoriasis, eczema, *etc.*) one of skill would understand the compounds treat the kerotic nature of the warts, not the viral infection.

This defect is not remedied by Poli *et al.* Poli *et al.* simply teach that **a 50% solution** of glycolic acid applied to viral cultures:

> Experiments were carried out at room temperature; **1 ml of each organic acid was mixed from time to time with 1 ml of the virus stock suspension** to be tested. [emphasis added] (see page 254)

However, a 50% solution of glycolic acid has a pH of about 1.3, substantially lower than the pH range of 2.45-4.6 recited in the pending claims.

The references offer no basis on which to infer that: 1) Gycolic acid at a higher pH will have antiviral activity; or 2) A glycolic acid formulation can be used as a prophylactic to prevent lesion formation.

Moreover, it is well recognized that glycolic acid is a skin irritant. As stated, for example, in Yu *et al.*:

> There is no doubt that alpha hydroxyacids, alpha ketoacids and related compounds are therapeutically effective for topical treatment of various cosmetic conditions and dermatologic disorders including dry skin, acne, dandruff, keratoses, age spots, wrinkles, skin lines and disturbed keratinization. However, **the compositions containing these acids may irritate human skin on repeated topical applications due to lower pH of the formulations. The irritation may range from a sensation of tingling, itching and burning to clinical signs of redness and peeling**. [emphasis added] (col. 2, lines 1-10)

Yu *et al.* then goes on to teach that their formulation, a combination of a an **amphoteric or pseudoamphoteric** compound; and **alpha hydroxyacids, alpha ketoacids** or related compound(s) overcomes this problem:

> It has now been discovered that amphoteric compositions containing alpha hydroxyacids, alpha ketoacids or related compounds, and also the compositions containing dimeric or polymeric forms of hydroxyacids overcomes the aforementioned shortcomings and retain the therapeutic efficacies for cosmetic conditions and dermatologic disorders. (col. 3, lines 10-16)

Moreover, recognizing the irritant nature of alpha hydroxyacids, alpha ketoacids Yu *et al.* teach away from a prophylactic application as recited in the present claims:

> For topical treatment of warts, keratoses, age spots, acne, nail infections, wrinkles or aging related skin changes, patients are advised to apply a small drop of the medication with a toothpick or a fine-caliber, commonly available artist's camel hair brush **to affected lesions only and not surrounding skin**. [emphasis added]

In contrast, the present application expressly teaches application to the surrounding tissue for perfection of infections (see, e.g., paragraph 0023 at page 6). This is captured in the amended claims which recite ". . . applying to an area of the skin."

Moreover, Yu *et al.* implicitly suggest that application of their formulation should be discontinued under the circumstances recited in the pending claim. In particular, claim 1 recites ". . . **said composition is applied during symptoms of pain, itching, burning, or tingling**", while Yu *et al.* teaches:

> For example, some clinical manifestations other than pain have been used as a signal to interrupt application. These manifestations include distinct blanching of the lesions or distinct peripheral erythema. (col. 12, lines 559-59)

Erythema (redness) would be expected to accompany burning and itching. Moreover, the langue recited above implies that pain is also a signal to interrupt application not a signal to go forward with treatment.

Yu *et al.* and Poli *et al.* thus fail to teach that glycolic acid has antiviral activity in the pH range recited in the claims. These references fail to teach or suggest that the presently claimed formulation has prophylactic activity. Moreover, the references teach that glycolic acid is a skin irritant, teach away from application to skin where lesions or keratoses are not present, and teach away from application under the conditions recited in the pending claims.

These defects are not remedied by Wenninger or the Merck Index. Wenninger is cited only as allegedly teaching that butylene glycol is useful as a solvent certain cosmetic products, and the Merck index is cited as allegedly teaching that the pH of 0.5% glycolic acid solution is 2.50.

The combination of Yu *et al.*, Poli *et al.*, Wenninger and the Merck index simply do not lead one of skill to the presently claimed method. Accordingly, the rejection on these grounds should be withdrawn.

Claims 1, 7-8, 15, and 24 were rejected under 35 U.S.C. §103(a) as allegedly obvious in view of Bhatia *et al.* (1998) *In. J. Animal Sci.* 68(6): 518-520 taken with Disinfectant Drugs (Therapeutic Programme Guidelines published by Health Canada) and Remington. Bhatia *et al.* is cited as allegedly teaching that 0.4 N hydrochloric acid is effective in inactivating sheep viruses. Disinfectant drugs is cited as teaching isopropanol for disinfecting contact lenses, while Remington is

cited as allegedly teaching ethanol and isopropanol as pharmaceutical solvents. Applicants traverse by argument and amendment.

In Bhatia *et al.*, the hydrochloric acid used to inactive goat pox virus in Bhatia *et al.* was 0.4%. A 0.4% solution of HCl should have a pH substantially lower than the pH range recited in the pending claims.

Moreover goat pox appears to be a relatively vulnerable virus. Bhatia *et al.*, for example teaches that sunlight inactivated the same virus:

> Sun light inactivated the virus in 60 min, whereas, the virus unexposed to sun light (kept in dark) when titrated had exposures respectively indicating 1×10^{33}, 1×10^{25} and 1×10^{15} GRD_{50}/0.2 ml residual titers.

Exposure to sunlight is not routinely used as a prophylactic for herpes virus. Indeed, to Applicants knowledge, sunlight is ineffective to kill Herpes virus. Thus, the goat-pox system appears to show unusual vulnerability to chemical and physical agents and does not inform one of skill as to the efficacy of antiviral compositions against other viruses or to the suitability for application of such compositions to the skin, or for the ability of such compositions to prophylactically prevent lesion formation as recited in the presently pending claims.

In addition, to the extent that Bhatia teaches the use of a virucide, it teaches away from the use of hydrochloric acid. As stated by Bhatia:

> Formalin and phenol completely inactivate the virus in 10 min, whereas hydrochloric did so in 30 min. . . . On the basis of the results obtained, **phenol in 2% concentration can be recommended for disinfecting** goat premises during goat-pox infection. Phenol is cheap, easily available and less irritant to tissues as compared to formalin.

In view of such teachings, one of skill in the art reading Bhatia *et al.* would be led to try phenol rather than hydrochloric acid in an antiviral formulation.

The defects of Bhatia *et al.* are not remedied by "Disinfectant Drugs", Remington, or any of the other cited references.

Disinfectant drugs simply teaches that isopropanol can be a component of a contact lens disinfectant. This reference does not teach that such a disinfectant has antiviral activity.

Moreover, to the extent that "Disinfectant Drugs" is taken as teaching the use of isopropanol, this reference teaches away from the present formulation. As shown in the Table on page

43 of this reference, **an acceptable concentration of isopropanol is given as ≥ 15%.** In the formulations recited in the presently pending claims, however, the alcohol is present at ". . . concentration of 0.2 to 13.0% . . . ". Thus, if "Disinfectant Drugs" is taken as teaching a formulation comprising isopropanol, the reference expressly directs one of skill away from the formulation recited in the pending claims. Remington teaches that ethanol and isopropanol are pharmaceutical solvents. This reference offers no teaching or suggestion that these alcohols are effective against virus or that these references can be combined with an acid to produce a virucide. Moreover, the combination of the cited art offers no teaching and fails to lead one of skill to the expectation that the compositions recited in the claims are prophylactic to prevent lesion formation. These references teach away from the concentration ranges cited in the claims, teach that acids are irritants and generally should not be applied to skin (*see,* Yu *et al., supra*). Accordingly, the cited references simply do not lead one of skill to the presently claimed methods. The Examiner has failed to make his *prima facie* case and the rejections under 35 U.S.C. §103(a) should be withdrawn.

Interview

Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor. Accordingly PTO Form PTOL-413A requesting discussion regarding the rejection under 35 U.S.C. §103(a) is provided herewith.

Conclusion

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 267-4161.

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Respectfully submitted,

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